

regards as the invention. Specifically, claim 1 has been rejected as being incomplete for omitting essential steps. This rejection is traversed in view of the following.

The Examiner's position is that a step should be included to describe the way in which the reaction of the liquid sample and an analyte reacting reagent forms a solution of a first coil-forming peptide.

It is well settled that the "language of the claims, read in light of the specification" is to be considered when determining whether the claims are definite. *Allen Archery Inc. v. Browning Mfg. Co.*, 819 F.2d 1087, 2 USPQ 2d 1490, 1494 (Fed. Cir. 1987). "If the claims, read in the light of the specification, reasonably apprise those skilled in the art both of the utilization and scope of the invention, and if the language is as precise as the subject matter permits, the courts can demand no more." *North Am. Vaccine, Inc. v. American Cyanamid Co.*, 7 F.3d 1571, 28 USPQ 2d 1333, 1339 (Fed. Cir. 1993).

Applicants submit that the claims are definite when read in view of the specification. Specifically, it is clear from the specification that the step of reacting the liquid sample with an analyte-reaction reagent may generate a solution form of the first coil-forming peptide in a number of ways. Exemplary methods of forming the first coil-forming peptide are clearly described in the specification on at least page 4, line 33 – page 5, line 4.

The Examiner has also rejected the claim for being inconsistent with the preamble because there is no correlation step in the body of the claim to indicate the determination of analyte presence.

Claim 1 has been amended to recite that the signal is correlated to the presence of analyte. Support for the amendment may be found on, at least, page 1, line 22-23 of the specification.

Accordingly, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. §112, second paragraph.

III. Rejection Under 35 U.S.C. §103

Claims 1-10 were rejected under 35 U.S.C. §103 as being obvious over Lennox *et al.* (WO 97/41424). This rejection is respectfully traversed for the following reasons.

A. The Present Invention

The present invention relies on three key features, none of which is shown or suggested in the cited prior art:

- i. producing a mobile "surrogate analyte" (the solution form of the coil-forming peptide) in an amount related to the amount of analyte, for reacting with the biosensor;
- ii. determining the presence or amount of analyte from a biosensor signal related to the amount of surrogate that binds to the biosensor; and
- iii. where the interaction of the surrogate with the biosensor is unrelated to the nature of the analyte.

These features provide several advantages over the biosensor methods and devices disclosed in the cited art. In particular,

1. the ability to detect both small- and large-molecule analytes in the same assay format.

In the methods described in the cited art, biosensor signal is based on the perturbation of the biosensor surface produced by the binding of an (relatively large) anti-ligand analyte to a (relatively small) ligand molecule carried on the biosensor surface. All assay formats in the prior art devices require this configuration. In the present invention, the size of the analyte is not crucial, since the method involves a biosensor responding to the interaction between two coil-forming peptides, not a ligand/anti-ligand interaction; and

2. the ability to design multi-analyte assays with a single type of biosensor. In the prior art, each biosensor requires an analyte-specific ligand carried on its surface. In the present invention, the method includes a biosensor having the same coil-forming peptide "receptor."

B. The Cited Art

Lennox (WO 97/41424) teaches a biosensor assay device for detecting a binding event between a ligand molecule attached to a biosensor surface and an anti-ligand molecule, whose binding to the biosensor-bound ligand perturbs the biosensor surface, producing a detectable biosensor signal. An array of biosensors is also disclosed. Nowhere does Lennox show or suggest the key features of the invention noted above, or the advantages achievable thereby.

C. Analysis

According to the MPEP §2143, "to establish a prima facie case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Third, the prior art reference (or references when combined) must teach or suggest all the claim limitations."

The Examiner's position is that Lennox teaches all of the limitations of the claim except for reacting the liquid sample with an analyte-reaction reagent. However, as noted above, Lennox fails to teach any of the key features of the claim. Even if these elements were disclosed in the cited reference, the prior art does not recognize the advantages of the invention, and thus provides no motivation for combining elements along the lines of the invention.

The Examiner also concludes that it would have been obvious to modify Lennox in such a way as to incorporate the analyte into the first coil-forming peptide before reaction with the second coil-forming peptide because it "would have had the advantage of requiring fewer steps to carry out the process of determination of analyte presence." The Examiner's position is not understood. As described on page 6, lines 18-24 of Lennox, two peptide subunits are constructed and assembled in a manner that anchors a ligand on the biosensor surface. The first peptide subunit is attached directly to the surface, and the second subunit is attached to the ligand. The next paragraph of the reference describes the two types of analyte-binding assays contemplated in the reference. The first is where the analyte is an antiligand molecule. In this case, the analyte can bind directly to the ligand molecule carried on the biosensor, to produce a biosensor signal. The second is where the analyte is a small-molecule (ligand). In this case, the assay further requires a ligand-binding agent that can bind both to the analyte and biosensor ligand. Thus, the reference requires two different assay formats for ligand and anti-ligand analytes, in contrast to the present invention.

Modification of the reference according to the Examiner's suggestion would still fail to produce the method of the invention. Lennox's invention, as described above, operates in a fundamentally different way than the present invention. If the analyte was incorporated into the first coil-forming peptide it is not clear how Lennox's invention would be used to determine the presence of analyte, or which steps should be left out of Lennox's process to achieve the claimed invention. The Examiner's rejection is not specific as to how one of ordinary skill in the art would have found it obvious to practice any specific method within the scope of the pending claims as of the filing date of the instant application.

In addition, the Examiner has provided no reference in support the assertion that it would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of Lennox et al. to obtain the claimed invention. If the Examiner wishes to support the assertion from personal experience, then such an assertion should be submitted in the form of an Examiner's affidavit. "When a rejection in an application is based on facts within the personal knowledge of an employee of the Office, the data shall be as specific as possible, and the

reference must be supported, when called for by the applicant, by the affidavit of such employee, and such affidavit shall be subject to contradiction or explanation by the affidavits of the applicant and other persons.” (37 C.F.R. 1.104(d)(2)).

The Examiner further asserts that “whether the analyte is contacted with the first coil-forming peptide before contact with the second peptide, or whether the analyte was contacted after heterodimer formation, the end result would have been the same, and one of ordinary skill in the art would have recognized that either protocol could have been used.” The Examiner appears to be implying that one of the two alternatives is found in the cited reference. However, neither alternative may be found in the Lennox reference. As described above, Lennox describes the two types of analyte-binding assays. The first is where the analyte is an antiligand molecule. In this case, the analyte can bind directly to the ligand molecule carried on the biosensor, to produce a biosensor signal. The second is where the analyte is a small-molecule (ligand). In this case, the assay further requires a ligand-binding agent that can bind both to the analyte and biosensor ligand. Thus, Lennox does not contact a first coil-forming peptide with an analyte either before or after heterodimer formation. The analyte contacts either a ligand or a ligand-binding agent.

For the reasons presented above, claim 1 cannot be considered obvious over the cited art or any other art known to the applicants. The remaining pending claims, which depend from claim 1, define over the cited art for the same reasons that claim 1 defines over the cited art.

Accordingly, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. §103.

IV. Conclusion

In view of the above remarks, Applicants submit that the claims now pending are in condition for allowance. A Notice of Allowance is, therefore, respectfully requested.

If in the opinion of the Examiner a telephone conference would expedite the prosecution of the subject application, the Examiner is encouraged to call the undersigned at (650) 838-4405.

Respectfully submitted,



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Version with Markings to Show Changes Made

In the Specification:

The paragraph beginning at line 29 of page 2 has been amended as follows:

Biosensors based on surface plasmon resonance (SPR) effects have also been proposed, for example, in U.S. Patent No. [Patents Nos.] 5,485,277 [and 6,492,840]. These devices exploit the shift in SPR surface reflection angle that occurs with perturbations, *e.g.*, binding events, at the SPR interface. Finally, a variety of biosensors that utilize changes in optical properties at a biosensor surface are known, *e.g.*, U.S. Patent No. 5,268,305.

In the Claims:

Claim 1 has been amended as follows:

1. (Twice Amended) A method for detecting or quantitating an analyte present in a liquid sample, comprising

reacting the liquid sample with an analyte-reaction reagent,

by said reacting, generating a solution of a first coil-forming peptide having a selected charge for interacting with a second, oppositely charged coil-forming peptide to form a stable α -helical coiled-coil heterodimer,

contacting the first coil-forming peptide generated by said reaction with a biosensor having a detection surface with surface-bound molecules of said second, oppositely charged coil-forming peptide, under conditions effective to form a stable α -helical coiled-coil heterodimer on said detection surface, where binding of the coil-forming peptide to the immobilized coil-forming peptide measurably alters a signal generated by the biosensor, [and]

measuring the signal generated by the biosensor to determine whether said coiled-coil heterodimer formation on said detector surface has occurred[.], and

correlating said generated signal to the presence of the analyte in the sample.